

23399

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference B. 11348 (B. 10476)	FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/EP2004/001471	International filing date (day/month/year) 17/02/2004	(Earliest) Priority Date (day/month/year) 21/02/2003
Applicant VAMA FARMACOSMETICA S.R.L.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☒ **Certain claims were found unsearchable** (See Box II).

3. ☐ **Unity of invention is lacking** (see Box III).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regards to the **drawings**,

a. the figure of the **drawings** to be published with the abstract is Figure No. _____

☐ as suggested by the applicant.

☐ as selected by this Authority, because the applicant failed to suggest a figure.

☐ as selected by this Authority, because this figure better characterizes the invention.

b. ☐ none of the figures is to be published with the abstract.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP2004/001471

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07C229/02 C07C59/245

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07C

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BEILSTEIN Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 914 326 A (GUSTIN JOHN ET AL) 22 June 1999 (1999-06-22) *abstract; columns 2-4 and the claims* -----	1-11
X	US 5 817 329 A (GARDINER PAUL T) 6 October 1998 (1998-10-06) *abstract; columns 3-5 and the claims* -----	1-11
X	MCCARTY M F: "PROMOTION OF HEPATIC LIPID OXIDATION AND GLUCONEOGENESIS AS A STRATEGY FOR APPETITE CONTROL" MEDICAL HYPOTHESES, EDEN PRESS, PENRITH, US, vol. 42, no. 4, 1994, pages 215-225, XP000654151 ISSN: 0306-9877 *abstract and pages 218-223* ----- -/--	1-11



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *G* document member of the same patent family

Date of the actual completion of the international search

23 July 2004

Date of mailing of the international search report

12/08/2004

Name and mailing address of the ISA

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Authorized officer

Lorenzo Varela, M.J.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP2004/001471

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 626 849 A (BARNES DAVID J ET AL) 6 May 1997 (1997-05-06) the whole document -----	1-11
X	FR 2 619 007 A (DERMATOLOGIQUES ET) 10 February 1989 (1989-02-10) *pages 1, 5-8 and the claims* -----	1-11
X	IT 1 217 516 B (SACCHETTI MASSIMO; CAROPRESE GIUSEPPE) 22 March 1990 (1990-03-22) the whole document -----	1-11
X	US 5 071 874 A (SCHOLL THOMAS ET AL) 10 December 1991 (1991-12-10) the whole document -----	1-11
X	FR 2 716 374 A (SEDERMA SA) 25 August 1995 (1995-08-25) the whole document -----	1-11
X	US 2002/106388 A1 (PUGLIESE PETER T) 8 August 2002 (2002-08-08) the whole document -----	1-11
X	DATABASE WPI Section Ch, Week 200109 Derwent Publications Ltd., London, GB; Class D13, AN 2000-062942 XP002289509 & NZ 330 439 A (IMMUNO LAB LTD) 26 January 2001 (2001-01-26) abstract -----	1-11

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2004/001471

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 10 and 11 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT .

Information on patent family members

International Application No

PCT/EP2004/001471

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 5914326	A	22-06-1999	AU 746157 B2	18-04-2002
			AU 8685798 A	01-03-1999
			CA 2340629 A1	18-02-1999
			CN 1272790 T	08-11-2000
			EP 1003529 A1	31-05-2000
			WO 9907388 A1	18-02-1999
US 5817329	A	06-10-1998	NONE	
US 5626849	A	06-05-1997	NONE	
FR 2619007	A	10-02-1989	FR 2619007 A1	10-02-1989
IT 1217516	B	22-03-1990	NONE	
US 5071874	A	10-12-1991	AT 93511 T	15-09-1993
			CA 2018137 A1	14-12-1990
			DD 295155 A5	24-10-1991
			DE 59002438 D1	30-09-1993
			DK 402755 T3	04-10-1993
			EP 0402755 A2	19-12-1990
			ES 2058680 T3	01-11-1994
			JP 3023919 B2	21-03-2000
			JP 3024010 A	01-02-1991
FR 2716374	A	25-08-1995	FR 2716374 A1	25-08-1995
US 2002106388	A1	08-08-2002	NONE	
NZ 330439	A	26-01-2001	AU 2907199 A	25-11-1999

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/EP2004/001471

International filing date (day/month/year)
17.02.2004

Priority date (day/month/year)
21.02.2003

International Patent Classification (IPC) or both national classification and IPC
C07C229/02, C07C59/245

Applicant
VAMA FARMACOSMETICA S.R.L.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITYInternational application No.
PCT/EP2004/001471

IAP8 Rec'd PCT/PTO 07 DEC 2005

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ in written format
 - ☐ in computer readable form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2004/001471

Box No. II Priority

1. ☒ The following document has not been furnished:

☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2004/001471

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. -

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the whole application or for said claims Nos. -

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form ☐ has not been furnished

☐ does not comply with the standard

the computer readable form ☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2004/001471

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-11
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	1-11
Industrial applicability (IA)	Yes: Claims	1-9
	No: Claims	

2. Citations and explanations

see separate sheet

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/EP2004/001471

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

For the assessment of the present claims 10 and 11 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

- D1: US-A-5 914 326 (GUSTIN JOHN ET AL) 22 June 1999 (1999-06-22)
- D2: US-A-5 817 329 (GARDINER PAUL T) 6 October 1998 (1998-10-06)
- D3: MCCARTY M F: "PROMOTION OF HEPATIC LIPID OXIDATION AND GLUCONEOGENESIS AS A STRATEGY FOR APPETITE CONTROL" MEDICAL HYPOTHESES, EDEN PRESS, PENRITH, US, vol. 42, no. 4, 1994, pages 215-225, XP000654151 ISSN: 0306-9877
- D4: US-A-5 626 849 (BARNES DAVID J ET AL) 6 May 1997 (1997-05-06)
- D5: FR-A-2 619 007 (DERMATOLOGIQUES ET) 10 February 1989 (1989-02-10)
- D6: IT-B-1 217 516 (SACCHETTI MASSIMO; CAROPRESE GIUSEPPE) 22 March 1990 (1990-03-22)
- D7: US-A-5 071 874 (SCHOLL THOMAS ET AL) 10 December 1991 (1991-12-10)
- D8: FR-A-2 716 374 (SEDERMA SA) 25 August 1995 (1995-08-25)
- D9: US 2002/106388 A1 (PUGLIESE PETER T) 8 August 2002 (2002-08-08)
- D10: DATABASE WPI Section Ch, Week 200109 Derwent Publications Ltd., London, GB; Class D13, AN 2000-062942 XP002289509 & NZ 330 439 A (IMMUNO LAB LTD) 26 January 2001 (2001-01-26)

1. The present application relates to hydroxy citrate carnitine salt, a preliposome for preparing dermo-cosmetic formulae for topical use containing carnitine hydroxy citrate, dermo-cosmetic formula for topical use prepared with a preliposome containing carnitine hydroxy citrate and the use of carnitine hydroxy citrate in the

treatment of cellulite and anomalous adiposity connected to this one and as food supplement.

2. D1 discloses compositions containing hydroxy citrate and carnitine and their use for promoting weight and fat loss (see the passages mentioned in the search report).
3. D2 discloses compositions containing hydroxy citric acid and carnitine and their use as a fat burning agent (see the passages mentioned in the search report).
4. D3 discloses compositions containing hydroxy citric acid and carnitine and their use as a fat burning agent. The synergetic effect of using both components is disclosed (see the passages mentioned in the search report).
5. D4 discloses compositions containing hydroxy citric acid and carnitine and their use as a weight loss agent.
6. D5 discloses salts of carnitine such as the salts of carnitine with citric acid, isocitric acid, alpha-cetoglutaric acid, succinic acid, fumaric acid, maleic acid and oxaloacetic acid and their use for the preparation of cosmetics and antilipidic agents (see the passages mentioned in the search report).
7. D6 discloses carnitine and its salts for the preparation of cosmetics useful in the treatment of cellulite.
8. D7 discloses carnitine magnesium citrate, a process for its production and its use in the preparation of food supplements.
9. D8 discloses hydroxy citric acid extracted from the plant "Garnicinia Cambogia" and its use in the preparation of dermo-cosmetics and antilipidc agents such as anticellulitic cosmetics.
10. D9 discloses carnitine and salts thereof useful in the treatment of cellulite.
11. D10 discloses compositions containing hydroxy citrate and carnitine and their use for promoting weight and fat loss.

Novelty

12. The subject-matter of claims 1-11 is novel in the sense of Art. 33(2) PCT. None of the available documents of the prior art discloses carnitine hydroxy citrate. Hence, preliposomes containing it or its use in the preparation of cosmetics or in the treatment of cellulite and adiposity connected to this or as a food supplement are novel as well.

Inventive step

13. The subject-matter of claims 1-11 cannot be considered to involve an inventive step in the sense of Art. 33(3) PCT.
- a. The use of a broad variety of carnitine salts and hydroxy citric acid in the preparation of cosmetics, in the treatment of cellulite and as food supplements is well known in the art (see (D5-D9).
- b. Furthermore, the use of compositions containing both carnitine/carnitine salts and hydroxy citric acid as a fat burning agent and the synergetic effect of using both components in the composition are known as well from D1-D4 and D10.
- c. Hence, the fact of using a salt obtained from both components: carnitine and hydroxy citric acid instead of using both components in a composition is an obvious possibility for the skilled person in the art. Inventive step could only be acknowledged if comparative examples are provided showing that the use of carnitine hydroxy citrate provides unexpected effects (better properties of the medicaments, cosmetics, food supplements) than the use of both components in the composition without forming the carnitine hydroxy citrate salt. As an evidence of such unexpected effects is not available at the moment, an inventive step cannot be acknowledged.

Further comments

14. Claims 10 and 11 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).
15. The use of the terms "similar types of cosmetics" in claim 9 and in the description leads to lack of clarity about the subject-matter for which protection is sought,

contrary to Art. 6 PCT. These terms should not have been used.

16. The use of the terms "and the like" in claim 11 as well as in the description leads to lack of clarity about the subject-matter for which protection is sought, contrary to Art. 6 PCT. These terms should not have been used.
17. The applicant reports in the application that the use of carnitine hydroxy citrate leads to better results than the use of only carnitine or only hydroxy citric acid. However, contrary to his arguments therein, the results of the test in which carnitine hydroxy citrate is used are not disclosed. Hence, there is no proof of having solved any technical problem.
18. The test data shown in table on page 9 are not clear. The meaning of the data therein is not clearly explained, contrary to Art. 6 PCT. The same objection arises for the table on page 10 wherein two different average values are given for each compound without providing any explanation concerning them.
19. The data in the graphics on pages 12-17 is not clearly disclosed, contrary to Art. 6 PCT. The reason therefore is that the different colours/granulation used in the graphics cannot be clearly seen.
20. There is a clerical mistake on page 1, "obsese subjects" is written therein instead of "obese subjects".
21. Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents D1-D10 is not mentioned in the description, nor are these documents identified therein.
22. When filing amended claims the applicant should at the same time bring the description into conformity with the amended claims.
23. In order to facilitate the examination of the conformity of the amended application with the requirements of Article 19 (2) and 34(2) b) PCT, the applicant is requested to clearly identify the amendments carried out, irrespective of whether they concern amendments by addition, replacement or deletion, and to indicate the passages of the application as filed on which these amendments are based.

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/EP2004/001471

If the applicant regards it as appropriate these indications could be submitted in handwritten form on a copy of the relevant parts of the application as filed.